Renal Tubular Acidosis

National Kidney and Urologic Diseases Information Clearinghouse

National Institute of Diabetes and Digestive and Kidney Diseases

NATIONAL INSTITUTES OF HEALTH

Your body's cells use chemical reactions to carry out tasks such as turning food into energy and repairing tissue. These chemical reactions generate acids. But too much acid in the blood—acidosis—can disturb many bodily functions. Healthy kidneys help maintain acid-base balance by excreting acids into the urine and returning bicarbonate—an alkaline, or base, substance—to the blood. This "reclaimed" bicarbonate neutralizes much of the acid that is created when food is broken down in the body.

Renal tubular acidosis (RTA) is a disease that occurs when the kidneys fail to excrete acids into the urine, which causes a person's blood to remain too acidic. Without proper treatment, chronic acidity of the blood leads to growth retardation, kidney stones, bone disease, and progressive renal failure.

One researcher, pediatric neurologist Donald Lewis, has theorized that Charles Dickens may have been describing a child with RTA when he created the character of Tiny Tim in his famous story, "A Christmas Carol." Tiny Tim's small stature, malformed limbs, and periods of weakness are all possible consequences of the chemical imbalance caused by RTA. Among the evidence cited to support this theory is the fact that Tiny Tim's condition, while fatal in one scenario, is reversible when Scrooge pays for medical treatments, which in those times would likely have included sodium bicarbonate and sodium citrate, which are alkaline agents that would neutralize the acid in Tiny Tim's blood. Whether the literary diagnosis of Tiny Tim is correct or not, the good news is that medical treatment can indeed reverse the effects of RTA.

Diagnosis

To diagnose RTA, your doctor will check the acid-base balance in samples of your blood and urine. If the blood is more acidic than it should be and the urine less acidic than it should be, RTA may be the reason, but additional information is needed first to rule out other causes. If RTA is suspected, additional information about the sodium, potassium, and chloride levels in the urine and the potassium level in the blood will help identify which of the three types of RTA you have. In all cases, the first goal of therapy is to neutralize acid in the blood, but different treatments may be needed to address the different underlying causes of acidosis.

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Types of RTA

At one time, doctors divided RTA into four types.

- Type 1 is also called classic distal RTA. "Distal," which means distant, refers to the point in the urine-forming tube where the defect occurs. It is relatively distant from the point where fluid from the blood enters the tiny tube, or *tubule,* that collects fluid and wastes to form urine.
- Type 2 is called proximal RTA. The word "proximal," which means near, indicates that the defect is closer to the point where fluid and wastes from the blood enter the tubule.
- Type 3 is rarely used as a classification today because it is now thought to be a combination of type 1 and type 2.
- Type 4 RTA is caused by another defect in the distal tubule, but it is different from classic distal RTA and proximal RTA because it results in high levels of potassium in the blood instead of low levels. Either low potassium (hypokalemia) or high potassium (hyperkalemia) can be a problem because potassium is important in regulating heart rate.

Type 1: Classic Distal RTA

This disorder may be inherited as a primary disorder or may be one symptom of a disease that affects many parts of the body. Researchers have now discovered the abnormal gene responsible for the inherited form. More often, however, classic distal RTA is a complication of diseases that affect many organ systems (systemic diseases), like the autoimmune disorders Sjögren's syndrome and lupus.

Other diseases and conditions associated with distal RTA include hyperparathyroidism, a hereditary form of deafness, analgesic nephropathy, rejection of a transplanted kidney, renal medullary cystic disease, obstructive uropathy, and chronic urinary tract infections.

A major consequence of classic distal RTA is low blood-potassium. The level drops if the kidneys excrete potassium into urine instead of returning it to the blood supply. Since potassium helps regulate nerve and muscle health and heart rate, low levels can cause extreme weakness, cardiac arrhythmias, paralysis, and even death.

Untreated distal RTA causes growth retardation in children and progressive renal and bone disease in adults. Restoring normal growth and preventing kidney stones, another common problem in this disorder, are the major goals of therapy. If acidosis is corrected with sodium bicarbonate or sodium citrate, then low blood-potassium, salt depletion, and calcium leakage into urine will be corrected. Alkali therapy also helps decrease the development of kidney stones. Potassium supplements are rarely needed except in infants, since alkali therapy prevents the kidney from excreting potassium into the urine.

Type 2: Proximal RTA

This form of RTA occurs most frequently in children as part of a disorder called Fanconi's syndrome. The symptoms of Fanconi's syndrome include high levels of glucose, amino acids, citrate, and phosphate in the urine, as well as vitamin D deficiency and low blood-potassium.

Proximal RTA can also result from inherited disorders that disrupt the body's normal breakdown and use of nutrients. Examples include the rare disease cystinosis (in which

cystine crystals are deposited in bones and other tissues), hereditary fructose intolerance, and Wilson's disease.

Proximal RTA also occurs in patients treated with ifosfamide, a drug used in chemotherapy. A few older drugs—such as acetazolamide or outdated tetracycline—can also cause proximal RTA. In adults, proximal RTA may complicate diseases like multiple myeloma, or it may occur in people who experience chronic rejection of a transplanted kidney.

When possible, identifying and correcting the underlying causes are important steps in treating the acquired forms of proximal RTA. The diagnosis is based on the chemical analysis of blood and urine samples. Children with this disorder would likely receive large doses of oral alkali, such as sodium bicarbonate or potassium citrate, to treat acidosis and prevent bone disorders, kidney stones, and growth failure. Correcting acidosis and low potassium levels restores normal growth patterns, allowing bone to mature while preventing further renal disease. Vitamin D supplements may also be needed to help prevent bone problems.

Type 4: Hyperkalemic RTA

This form of RTA is most often referred to as type 4. It occurs when blood levels of the hormone aldosterone are low or when the kidneys do not respond to it. Aldosterone directs the kidneys to regulate the levels of sodium, potassium, and chloride in the blood. Type 4 RTA is distinguished by a high blood-potassium level.

Hyperkalemic distal RTA may result from sickle cell disease, urinary tract obstruction, lupus, amyloidosis, or transplantation.

Aldosterone's action may be impeded by drugs, including

- diuretics used to treat congestive heart failure such as spironolactone or eplerenone
- blood pressure drugs called angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)
- the antibiotic trimethoprim
- an agent called heparin that keeps blood from clotting
- the antibiotic pentamidine, which is used used to treat pneumonia
- a class of painkillers called nonsteroidal anti-inflammatory drugs (NSAIDs)
- some immunosuppressive drugs used to prevent transplant rejection

For people who produce aldosterone but cannot use it, researchers have now identified the genetic basis for their body's resistance to the hormone. To treat type 4 RTA successfully, patients may require alkaline agents to correct acidosis as well as medication to lower the potassium in their blood.

If treated early, most people with RTA will not develop permanent kidney failure. Therefore, the goal is early recognition and adequate therapy, which will need to be maintained and monitored throughout the patient's lifetime.

Hope Through Research

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports research into many kinds of kidney disease, including renal tubular acidosis. NIDDK-supported researchers are exploring the genetic and molecular mechanisms that control acid-base regulation in the kidney. These studies will point the way to more effective treatments for RTA.

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Publications produced by the Clearinghouse are carefully reviewed by both NIDDK scientists and outside experts.

This fact sheet is also available at *www.kidney.niddk.nih.gov.*

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